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Full Length Article

Small intestinal cancers among adults in an Egyptian district: A clinicopathological study using a population-based cancer registry

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KEYWORDS

Egypt;
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Abstract *Background:* Small intestinal cancers (SICs) are very rare all over the world and little is known about them in Egypt.
Methods: This a retrospective study. Between 2000 and 2002, 30 cases with SICs were identified in the Gharbiah population based cancer registry (GPBCR); 17 cases of whom were treated at Tanta Cancer Center (TCC).
Results: The median age was 51 years with female predominance. The duodenum was the commonest site (43%) followed by the ileum then the jejunum. Adenocarcinoma (AC), carcinoids, gastrointestinal stromal tumors (GISTs), lymphoma and sarcoma represented 50%, 10%, 17%, 13% and 10% respectively. Abdominal pain was the commonest symptom and localized disease was the commonest presentation. Surgery, chemotherapy and radiotherapy were employed in 65%, 35% and 0% of patients, respectively. The median overall survival and progression free survival (OS, PFS) were 18 and 15 months (95% CI: 10.4–25.6 and 3.6–26.4), respectively. AC had inferior OS and PFS to other histologies ($p = 0.08$ and 0.12, respectively). Also, duodenum subsite was inferior in OS and PFS to other sites ($p = 0.25$ and 0.35, respectively).

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Conclusions: SICs in Gharbiah, Egypt are characterized by predominance of female gender and adenocarcinoma histology. One year survival is 64% with a poor outcome for adenocarcinoma and duodenal subsite.

Introduction

Despite the small intestine being the longest part of the bowel, small intestinal cancer (SIC) is a rare disease compared to cancer in shorter parts like the colon and the stomach. SICs account for less than 5% of gastrointestinal cancers (GITCs) [1]. Differences in microbial flora, metabolism of bile acids, and transit time may account for the variation [2]. The risk factors for SICs include cigarette smoking, alcohol intake, and other medical conditions including Chron's disease and familial adenomatous polyposis (FAP), cholecystectomy, peptic ulcer disease, and cystic fibrosis [1].

SICs show geographical, sex, age, racial and temporal variations in different parts of the world [1,3]. Age-standardized rates (ASRs) per 100,000 population vary from 0.1 in Zimbabwe to 3 in the USA. Male predominance is the commonest where female predominance is noticed occasionally [3]. The incidence increases with age and blacks have higher ASR than whites [2,4]. Moreover, many authors reported rising incidences of SICs [1,2,4]. The geographical and temporal variations suggest that environmental factors play an important role in the etiology of SICs [1].

Little is known about SICs in Egypt. Thus, we conducted this study to recognize the clinicopathological features, presentations, treatments and outcomes of SICs in Egypt.

Methods

This is a retrospective study. Patients with SICs were identified through the Gharbiah population based cancer registry (GPBCR). Data on age, sex, sub-site, histology, grade, stage and treating center were obtained from the registry. Further data on complaints, comorbidities, treatment modalities, relapse, dates of diagnosis, surgery and relapse, and survival were obtained for those subset of patients treated at Tanta Cancer Center (TCC). The study was approved by the IRB of the Egyptian National Cancer Institute.

Inclusion criteria were adult patients (age of 18 years or more) with SIC and a confirmed malignant histology between 2000 and 2002. Exclusion criteria were non-confirmed histologic subtype as those diagnosed based on death certificate, radiology or unspecified malignant type.

Between 2000 and 2002, 34 cases with SICs contained GPBCR were identified. Four cases of which were excluded

Table 1 Characteristics of 30 patients with small intestinal cancers histologically confirmed at GPBCR including 17 cases treated at TCC.

Characteristic	GPBCR cases number (%)	TCC cases number (%)	Non-TCC cases number (%)	*P* value
Total	30 (100)	17 (100)	13 (100)	
Sex				
Male	12 (40)	7 (41)	5 (39)	
Female	18 (60)	10 (59)	8 (61)	0.88
Site				
Duodenum	13 (43)	7 (41)	6 (46)	
Jejunum	4 (13)	4 (24)	0 (0)	
Ileum	6 (20)	1 (6)	5 (39)	
NOS	7 (24)	5 (29)	2 (15)	0.24
Histology				
Adenocarcinoma	15 (50)	9 (53)	6 (46)	
Malignant carcinoid	3 (10)	1 (6)	2 (15)	
NHL	4 (13)	1 (6)	3 (24)	
GIST	5 (17)	3 (18)	2 (15)	
Leiomyosarcoma	3 (10)	3 (18)	0 (0)	0.81
SEER Stage				
Localized	14 (47)	11 (65)	3 (24)	
Regional	7 (23)	1 (6)	6 (46)	
Distant	5 (17)	5 (29)	0 (0)	
Unknown	4 (13)	0 (0)	4 (30)	0.01

GPBCR: Gharbiah population based cancer registry, TCC: Tanta Cancer Canter, NOS: not otherwise specified, SEER: Surveillance Epidemiology and End Results, NHL: non-Hodgkin's lymphoma, GIST: gastrointestinal stromal tumor.

being diagnosed based on the death certificates, radiologic appearance or clinical findings during exploration with no histopathological confirmation.

Statistical analysis

All analyses were done using SPSS® software program version 15 (Chicago, USA). Nominal and categorical data were compared for different histologies (adenocarcinoma (AC) vs. non-AC) and subsite (duodenum vs. others) using the Chi squared test. Survival was calculated using the Kaplan Meyer methods and groups were compared using the log-rank test. A probability (p) equal to or less than 0.05 (two sided) was considered statistically significant.

Results

SICs represented 4% of GIT cancers. The median age was 51 years (range, 20–78 years). Female predominance was noticed (1.5:1) and this predominance was noticed with duodenum and other subsites, and with Adenocarcinoma (AC), gastro-intestinal stromal tumors (GIST) and leiomyosarcoma but not with carcinoids or lymphoma. The duodenum was the commonest involved site (43%). However, the site was not mentioned in one quarter of cases. AC was the commonest histology (50%) while malignant carcinoids were encountered in 3 cases. There were 4 cases of non-Hodgkin's lymphoma; two were diffuse large B-cell type, one marginal zone type and one unspecified. There were 5 cases of GIST and three of them were low-grade. Most (10/13) of duodenal tumors (69%) were ACs and most (10/15) of ACs affected the duodenum (67%). Most of non-AC (75%) affected the jejunum and ileum. Table 1 shows the characteristics of patients involved in the current study. Most patients had a non-metastatic disease either local or regional. Metastases were documented at initial presentation in five patients. All involved the liver with the pancreas being additionally involved in one case.

Clinical data particularly pertaining to treatment and follow up, other than those mentioned previously, were not contained in GPBCR. Thus we tried to further track as much cases as possible through reviewing cases that presented to TCC, the main oncology center in Gharbiah governorate, Egypt. We could identify 17 cases whose information is discussed below in more detail.

TCC cases were similar to those of GPBCR. TCC cases had higher local and distant diseases and a lower regional disease than non-TCC cases ($P = 0.01$; Table 1). Otherwise, TCC and non-TCC cases were not significantly different. Most TCC patients had symptoms related to their disease with abdominal pains being the commonest. One third of the patients had concurrent co-morbidities; diabetes (2/6), hypertension (2/6), both (1/6) and hepatic cirrhosis (1/6).

While none received radiotherapy, most patients (65%) underwent surgery that was definitive (9/11) or palliative (4/11). One third of patients received chemotherapies that were 5-fluorouracil based in patients with AC (4/6), CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone) in one case with NHL and doxorubicin in one case with leiomyosarcoma. For patients with AC, chemotherapy was given adjuvantly for node positive disease in two patients and palliatively in the metastatic setting of two patients. Only 4 patients had documented relapses that were local in all cases (Table 2).

Table 2 More details on 17 patients with small intestinal cancers who presented to Tanta Cancer Canter.

Characteristic	Number	%
Complaints		
Abdominal pains only	7	41
Intestinal obstruction	2	12
Vomiting and pains	2	12
Diarrhea	2	12
None/unknown	4	23
Co-morbidities		
No	6	35
Yes	6	35
Unknown	5	30
Surgery		
Yes	11	65
No	3	17.5
Unknown	3	17.5
Chemotherapy		
Yes	6	35
No	8	47
Unknown	3	18
Chemotherapy regimens		
5-FU based	4	23
CHOP	1	6
Doxorubicin	1	6
None	11	65
Relapses (12 cases)*		
Yes	4	33
No	5	42
Unknown	3	25

* 5 patients were metastatic at initial presentation and not included here. 5-FU: 5- fluorouracil, CHOP: cyclophosphamide, doxorubicin, vincristine, prednisolone.

After a median follow up of 26 months (range 25–104), 4/17 patients relapsed and 11/17 were dead. Deaths were disease related in 9/11 cases. The median overall survival (OS) was 18 months (95% CI 10.4–25.6; Figure 1). The one- and two-year OS rates were 64% and 38%, respectively. The median progression free survival (PFS) was 15 months (95% CI 3.6–26.4; Figure 2). The one- and two-year PFS survival rates were 51% and 32%, respectively.

Comparing AC to non-AC histology showed that both OS and PFS were inferior in the AC group. The one- and two-year OS for AC were 56% and 22% and for non-AC were 73% and 58%, respectively. The one- and two-year PFS for AC were 44% and 22% and for non-AC were 58% and 43%, respectively. However, the differences were not statistically significant ($p = 0.08$ and 0.12; Figures. 3 and 4, respectively). Comparing SIC subsites showed that both OS and PFS were inferior for the duodenum than other subsites. The one- and two-year OS for duodenal site were 43% and 29% and for non-duodenal sites were 68% and 45%, respectively. The one- and two-year PFS for duodenal site were 43% and 43% and for non-duodenal sites were 67% and 34%, respectively. However, the differences were not statistically significant ($p = 0.25$ and 0.35; Figures. 5 and 6 respectively).

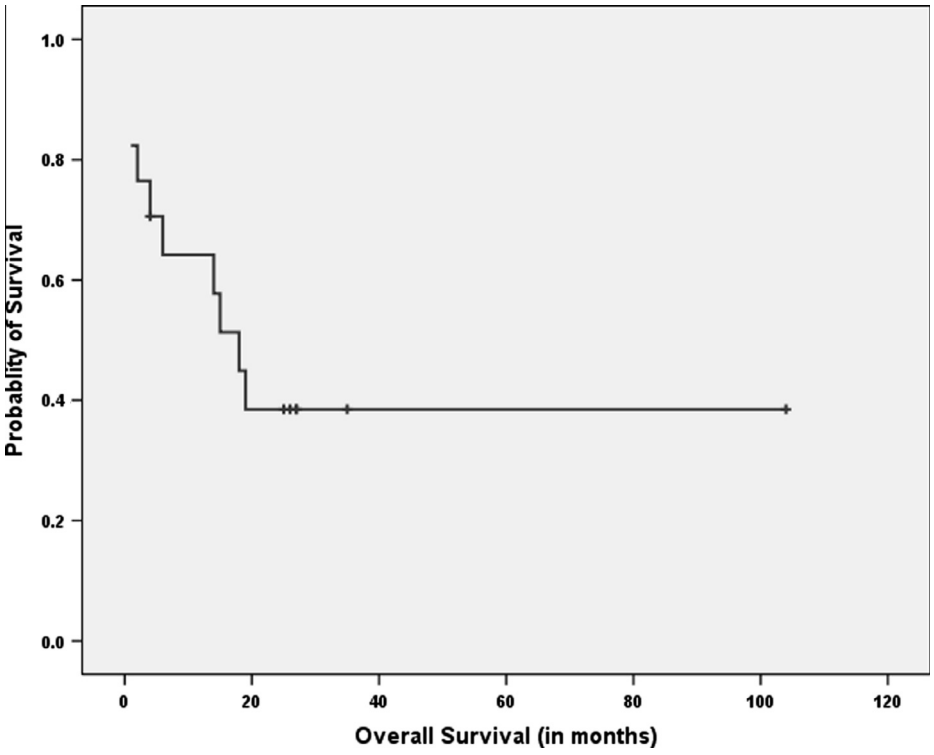

Figure 1 Overall survival in 17 patients with small intestinal cancers.

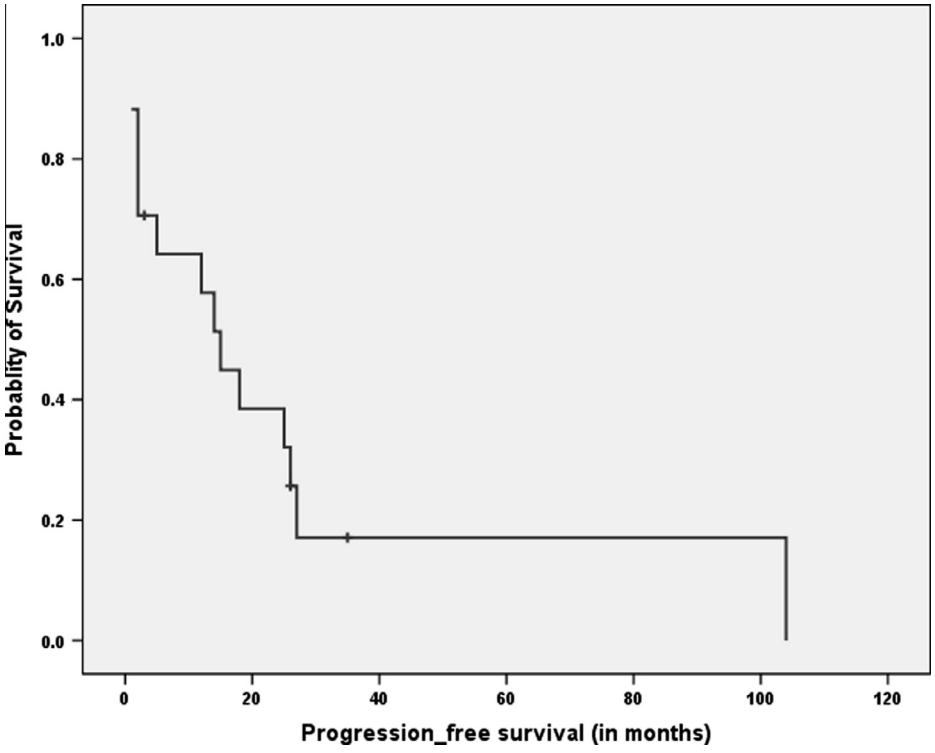

Figure 2 Progression-free survival of 17 patients with small intestinal cancer.

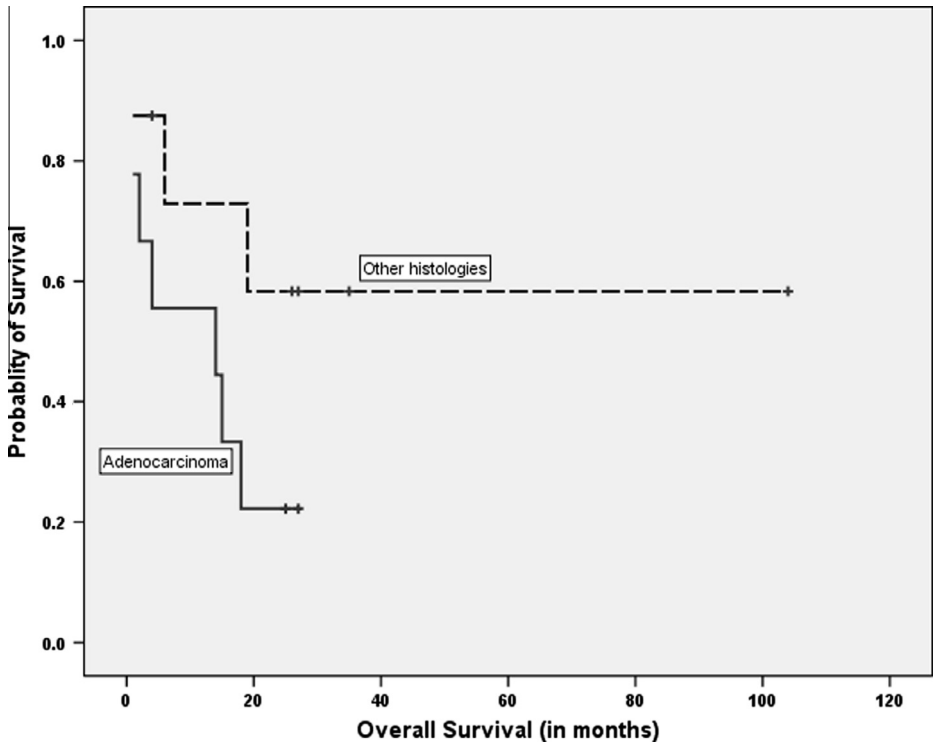

Figure 3 Overall survival in patients with adenocarcinoma vs. other cancers of the small intestine ($p = 0.12$).

Discussion

Despite the relatively small numbers, this is the first population-based study comprehensively reporting SICs in Egypt particularly the information related to treatments and their outcomes including recurrences and survival.

In Egypt, SICs represented 4% of GI cancers and 0.8% of the total cancers comparable to 3.6% and 0.5% in the USA [5]. ASRs of SICs in Egypt are similar to those in many countries [3,6,7]. However, age of SICs in Egypt is one decade below that of industrialized countries like the USA [1]. Age differences between Egypt and Western countries were also noted in many cancers including breast cancer, colon cancer and liver cancer [8–11]. This age difference may be explained by differences in population structures with lower life expectancy and younger median population age among Egyptians compared to Western countries [12,13].

Sex variation of SICs across different geographic regions is reported in the literature [2,3,14–18]. Similar to reports from Hawaii, Philippines, French Polynesia, Russia St. Petersburg, Spain Cuenca, Turkey Izmir, Kuwait and some areas of Switzerland, the current study showed that females are more affected than males, [3,14]. However, other authors showed a reverse pattern in North America and Europe [2,15–18]. Most of the registries that showed female predominance, like ours, reported on small SIC numbers mostly in less developed regions and those showing male predominance reported on big numbers in more developed regions [3]. Female predominance in the current study, in contrast with male predominance in bigger reports from Western countries, could be reasoned by differences in genetic constitutions, susceptibilities and exposure to risk factors. Obesity and alcohol were mentioned in many reports to be risk factors for SICs [19–24]. Thus, differences in obesity and alcohol intake might partially explain for the SIC' sex variation between Egypt and Western countries. Almost 72% of women and 50% of men in Egypt were overweight or obese [25] compared to a reverse pattern in the US (57% in females and 70% in males) [26]. While drinking alcoholic beverages is occasional among Egyptian males and females [27], almost 87% of US males and 63% of US females drink alcohol [28]. Thus, the more alcoholic drinking and obesity in males might explain for the predominance of SICs in males, while the paucity of alcohol use in Egyptian males and females may lead the overweight issue to be a key player to get male SIC predominance among Egyptians.

SICs in Egypt, as shown in this study, are characterized by a higher incidence of AC, resembling industrialized countries, and a lower incidence of lymphoma unlike the developing countries [1]. While the percentages of sarcomas and lymphomas in the current study are similar to those from other population-based cancer registries from the USA [2,29,30], England & Wales and Scotland [4], the incidence of malignant carcinoids was lower and that of AC which was higher. While this could be a true finding related to genetic, racial or environmental factors, it may reflect under diagnosis of carcinoids and over diagnosis of AC. Some cases of carcinoids may be diagnosed as AC. This can be plausible particularly that carcinoid diagnosis is not a sole light microscopical diagnosis for the most part, but rather a multidisciplinary diagnostic model using biochemical analysis, standard cross-sectional imaging, newer advances in nuclear medicine and immunohistochemical studies [31]. This may also be a random variation associated with relatively low number of cases [4]. Also, exclusion of pediatric SICs may have contributed to the underrepresentation of lymphomas.

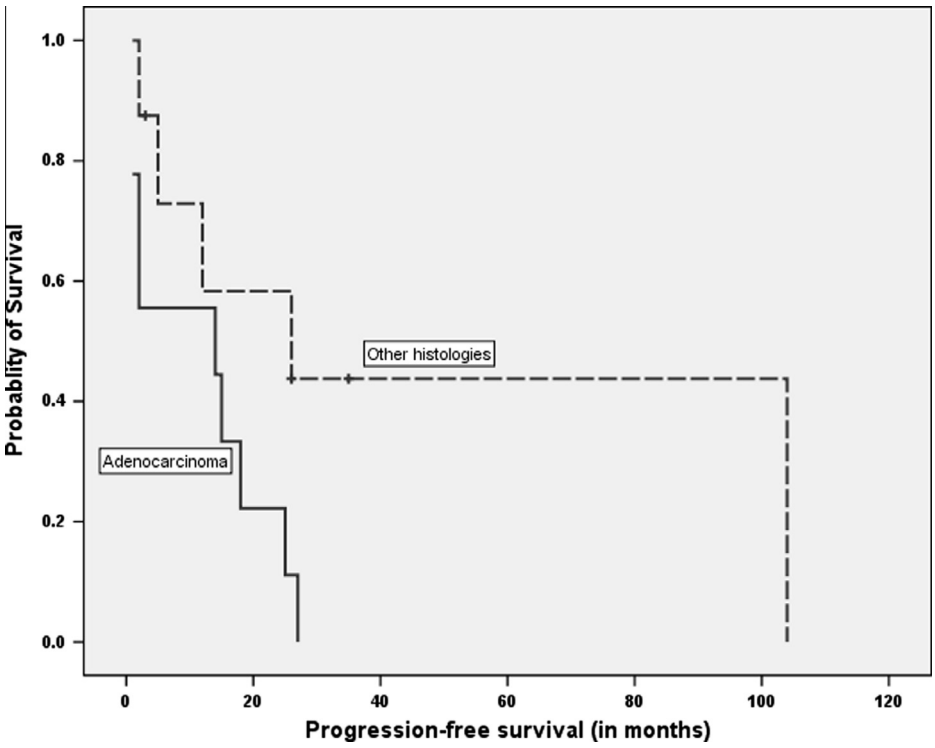

Figure 4 Progression-free survival in patients with adenocarcinoma vs. other cancers of the small intestine ($p = 0.08$).

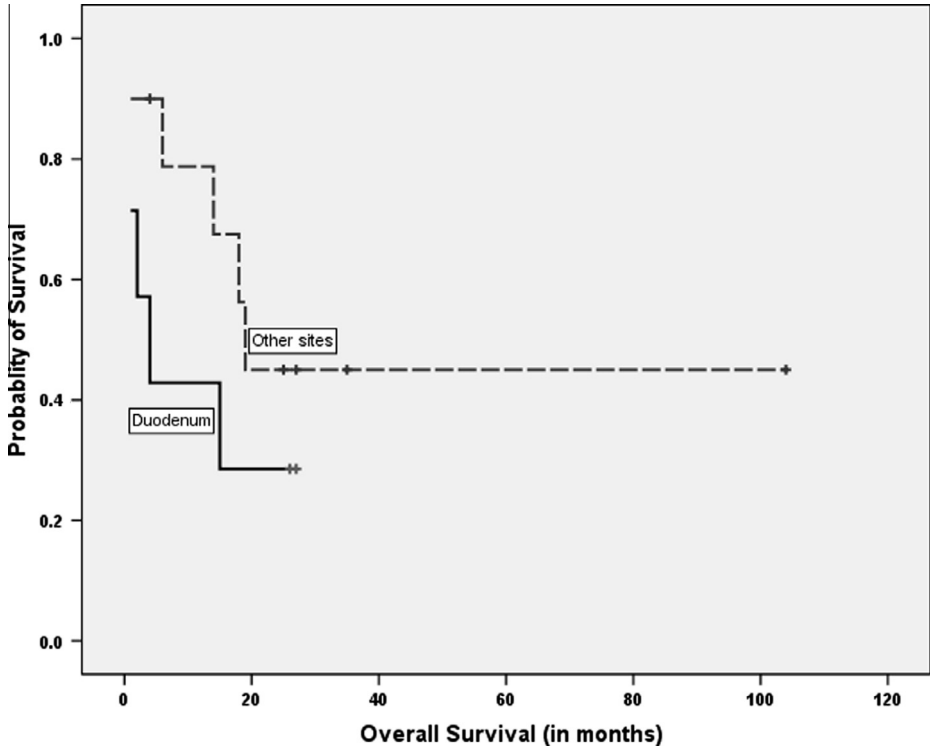

Figure 5 Overall survival of small intestinal cancer according to subsite; duodenum vs. other sites ($p = 0.25$).

Similar to reports from the USA, England & Wales and Scotland [4,29], we showed that the duodenum was the commonest subsite followed by the ileum and then the jejunum. While the percentage of jejunal and SICs NOS (not otherwise specified) in the current study was similar to that from other population-based cancer registries from the USA [1,2], the percentage of ileal SICs was lower and that of duodenal SICs was higher. The reason for this is unknown. However, the

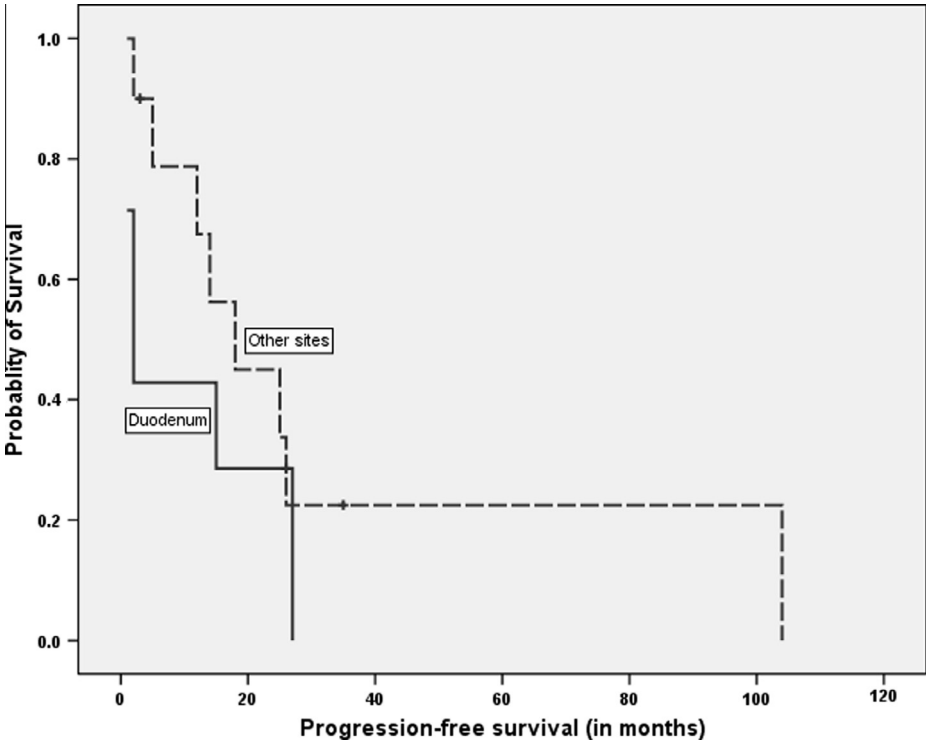

Figure 6 Progression-free survival in small intestinal cancers according to subsite; duodenum vs. other sites ($p = 0.35$).

small numbers in the current study may have an exaggerating effect on the percentage. Also, racial and environmental factors could be players.

Site and histology are linked as most of carcinoids being located in the ileum and most ACs being located in the duodenum [1]. In the current study, only 20% of SICs affected the ileum and this was reflected on paucity of carcinoids. Also, the small absolute numbers in the current study together with exclusion of 4 cases with unknown histology can partly explain for that. However, ethnic, genetic and environmental factors [2,3] as well as geographical variations [3] may contribute to the differences.

The OS in our study is similar to that from Scotland and England & Wales [4]. The one year OS (64%) is similar to reports from the USA (74%) [2]. Similar to Qubaiah and his colleagues, we showed that the OS of AC and duodenal subite were less favorable than other histologies and subsites [2]. The worse outcome of duodenal cancers despite the potential for early detection may relate to the dominance of aggressive cancers (ACs vs. other histologies) that may be less responsive to therapeutic interventions including technical difficulties for surgical resection [2].

In conclusion, SICs are a rare disease among adult Egyptians residing in Gharbiah district. It is characterized by predominance of female gender, duodenal site and adenocarcinoma histology. Surgery is the main therapeutic modality and chemotherapy was infrequently encountered. Survival outcomes are comparable to other populations.

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Conflict of interest

None declared.

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